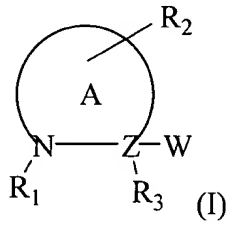
In the claims:

For the convenience of the Examiner, all claims being examined, whether or not amended, are presented below.

1. (Currently Amended) A method for ~~modifying~~reduciing the rate of ~~, in an animal,~~ metabolism of glucagon-like peptide 1 (GLP-1), comprising administering to ~~the~~ an animal a composition including one or more inhibitors of ~~a~~ dipeptidylpeptidase IV~~which inactivates GLP-1~~, wherein the inhibitor is represented by Formula I:



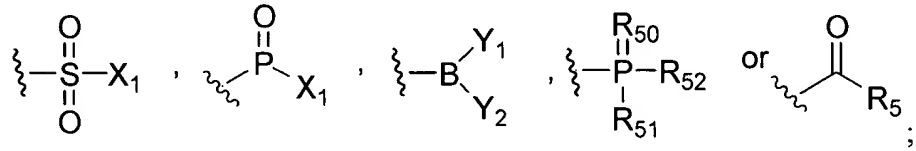
(I)

wherein

A represents a 4-8 membered heterocycle including the N and a Cα carbon;

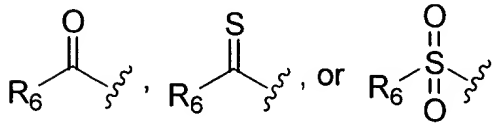
Z represents C or N;

W represents -CH=NR5, ~~a functional group which reacts with an active site residue of the targeted protease, or~~



;

R_1 represents a C-terminally linked amino acid residue or amino acid analog, or a C- terminally linked peptide or peptide analog, or an amino-protecting group, or



;

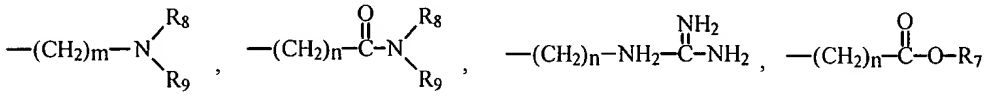
R_2 is absent or represents one or more substitutions to the ring A, each of which can independently be a halogen, a lower alkyl, a lower alkenyl, a lower alkynyl, a carbonyl, a

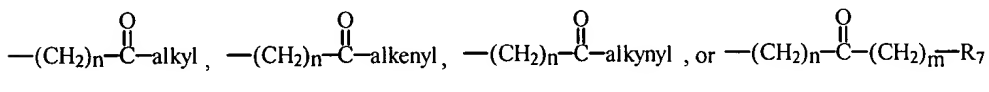
thiocarbonyl, an amino, an acylamino, an amido, a cyano, a nitro, an azido, a sulfate, a sulfonate, a sulfonamido, -$(CH_2)_m$-R_7, -$(CH_2)_m$-OH, -$(CH_2)_m$-O-lower alkyl, -$(CH_2)_m$-O-lower alkenyl, -$(CH_2)_n$-O-$(CH_2)_m$-R_7, -$(CH_2)_m$-SH, -$(CH_2)_m$-S-lower alkyl, -$(CH_2)_m$-S-lower alkenyl, or -$(CH_2)_n$-S-$(CH_2)_m$-R_7;

if Z is N, R_3 represents hydrogen, if Z is C, R_3 represents hydrogen or a halogen, a lower alkyl, a lower alkenyl, a lower alkynyl, a carbonyl, a thiocarbonyl, an amino, an acylamino, an amido, a cyano, a nitro, an azido, a sulfate, a sulfonate, a sulfonamido, -$(CH_2)_m$-R_7, -$(CH_2)_m$-OH, -$(CH_2)_m$-O-lower alkyl, -$(CH_2)_m$-O-lower alkenyl, -$(CH_2)_n$-O-$(CH_2)_m$-R_7, -$(CH_2)_m$-SH, -$(CH_2)_m$-S-lower alkyl, -$(CH_2)_m$-S-lower alkenyl, or -$(CH_2)_n$-S-$(CH_2)_m$-R_7;

R_5 represents a hydrogen, an alkyl, an alkenyl, an alkynyl, -$C(X_1)(X_2)X_3$, -$(CH_2)_m$-R_7, -$(CH_2)_n$-OH, -$(CH_2)_n$-O-alkyl, -$(CH_2)_n$-O-alkenyl, -$(CH_2)_n$-O-alkynyl, -$(CH_2)_n$-O-$(CH_2)_m$-R_7, -$(CH_2)_n$-SH, -$(CH_2)_n$-S-alkyl, -$(CH_2)_n$-S-alkenyl, -$(CH_2)_n$-S-alkynyl, -$(CH_2)_n$-S-$(CH_2)_m$-R_7, -C(O)C(O)NH_2, or -C(O)C(O)OR'$_7$;

R_6 represents hydrogen, a halogen, ~~an~~ an alkyl, ~~an~~ an alkenyl, ~~an~~ an alkynyl, an aryl, -$(CH_2)_m$-R_7, -$(CH_2)_m$-OH, -$(CH_2)_m$-O-alkyl, -$(CH_2)_m$-O-alkenyl, -$(CH_2)_m$-O-alkynyl, -$(CH_2)_m$-O-$(CH_2)_m$-R_7, -$(CH_2)_m$-SH, -$(CH_2)_m$-S-alkyl, -$(CH_2)_m$-S-alkenyl, -$(CH_2)_m$-S-alkynyl, ~~or~~ -$(CH_2)_m$-S-$(CH_2)_m$-R_7,





;

R_7 represents, for each occurrence, a substituted or unsubstituted aryl, aralkyl, cycloalkyl, cycloalkenyl, or heterocycle;

R'$_7$ represents, for each occurrence, hydrogen, or a substituted or unsubstituted alkyl, alkenyl, aryl, aralkyl, cycloalkyl, cycloalkenyl or heterocyclyl;

R_8 and R_9 each independently represent hydrogen, alkyl, alkenyl, $-(CH_2)_m-R_7$, -C(=O)-alkyl, -C(=O)-alkenyl, -C(=O)-alkynyl, or $-C(=O)-(CH_2)_m-R_7$,

or R_8 and R_9 taken together with the N atom to which they are attached complete a heterocyclic ring having from 4 to 8 atoms in the ring structure;

R_{50} represents O or S;

R_{51} represents N_3, SH, NH_2, NO_2 or OR'7;

R_{52} represents hydrogen, a lower alkyl, an amine, OR'7, or a pharmaceutically acceptable salt, or R_{51} and R_{52} taken together with the phosphorous atom to which they are attached complete a heterocyclic ring having from 5 to 8 atoms in the ring structure;

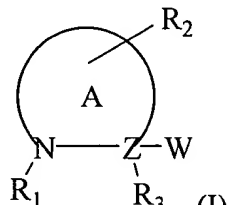
Y_1 and Y_2 can independently or together be a group capable of being hydrolyzed to a hydroxyl group, or cyclic derivatives where Y_1 and Y_2 are connected via a ring having from 5 to 8 atoms in the ring structure;

X_1 represents a halogen;

X_2 and X_3 each represent a hydrogen or a halogen;

m is zero or an integer in the range of 1 to 8; and n is an integer in the range of 1 to 8.

2. (Currently Amended) A method for ~~modifying~~ improving glucose ~~metabolism of an animal~~tolerance, comprising administering to ~~the~~ an animal a composition including one or more protease inhibitors which inhibit ~~DPIV-mediated proteolysis~~dipeptidylpeptidase IV, wherein the inhibitor is represented by Formula I:



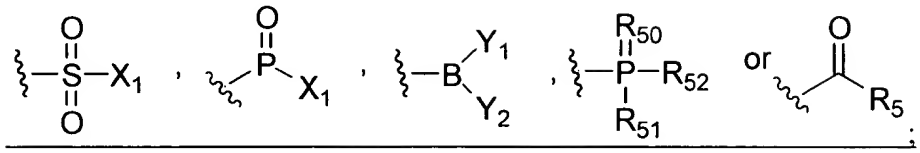
(I)

wherein

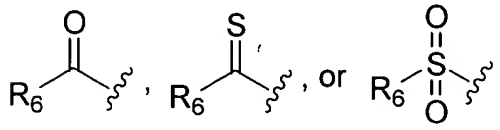
A represents a 4-8 membered heterocycle including the N and a Cα carbon;

Z represents C or N;

W represents -CH=NR$_5$,



R$_1$ represents a C-terminally linked amino acid residue or amino acid analog, or a C- terminally linked peptide or peptide analog, or an amino-protecting group, or



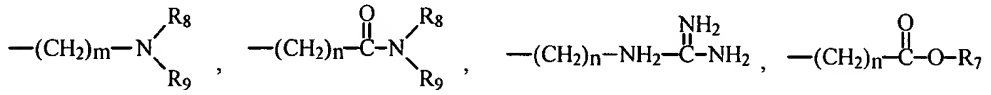
R$_2$ is absent or represents one or more substitutions to the ring A, each of which can independently be a halogen, a lower alkyl, a lower alkenyl, a lower alkynyl, a carbonyl, a thiocarbonyl, an amino, an acylamino, an amido, a cyano, a nitro, an azido, a sulfate, a sulfonate, a sulfonamido, -(CH$_2$)$_m$-R$_7$, -(CH$_2$)$_m$-OH, -(CH$_2$)$_m$-O-lower alkyl, -(CH$_2$)$_m$-O-lower alkenyl, -(CH$_2$)$_n$-O-(CH$_2$)$_m$-R$_7$, -(CH$_2$)$_m$-SH, -(CH$_2$)$_m$-S-lower alkyl, -(CH$_2$)$_m$-S-lower alkenyl, or -(CH$_2$)$_n$-S-(CH$_2$)$_m$-R$_7$;

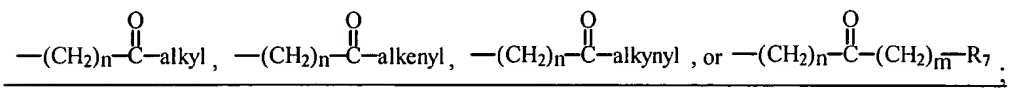
if Z is N, R$_3$ represents hydrogen, if Z is C, R$_3$ represents hydrogen or a halogen, a lower alkyl, a lower alkenyl, a lower alkynyl, a carbonyl, a thiocarbonyl, an amino, an acylamino, an amido, a cyano, a nitro, an azido, a sulfate, a sulfonate, a sulfonamido, -(CH$_2$)$_m$-R$_7$, -(CH$_2$)$_m$-OH, -(CH$_2$)$_m$-O-lower alkyl, -(CH$_2$)$_m$-O-lower alkenyl, -(CH$_2$)$_n$-O-(CH$_2$)$_m$-R$_7$, -(CH$_2$)$_m$-SH, -(CH$_2$)$_m$-S-lower alkyl, -(CH$_2$)$_m$-S-lower alkenyl, or -(CH$_2$)$_n$-S-(CH$_2$)$_m$-R$_7$;

R$_5$ represents a hydrogen, an alkyl, an alkenyl, an alkynyl, -C(X$_1$)(X$_2$)X$_3$, -(CH$_2$)$_m$-R$_7$, -(CH$_2$)$_n$-OH, -(CH$_2$)$_n$-O-alkyl, -(CH$_2$)$_n$-O-alkenyl, -(CH$_2$)$_n$-O-alkynyl, -(CH$_2$)$_n$-O-(CH$_2$)$_m$-R$_7$, -(CH$_2$)$_n$-SH, -(CH$_2$)$_n$-S-alkyl, -(CH$_2$)$_n$-S-alkenyl, -(CH$_2$)$_n$-S-alkynyl, -(CH$_2$)$_n$-S-(CH$_2$)$_m$-R$_7$, -C(O)C(O)NH$_2$, or -C(O)C(O)OR'$_7$;

R$_6$ represents hydrogen, a halogen, an alkyl, an alkenyl, an alkynyl, an aryl, -(CH$_2$)$_m$-R$_7$, -(CH$_2$)$_m$-OH, -(CH$_2$)$_m$-O-alkyl, -(CH$_2$)$_m$-O-alkenyl, -(CH$_2$)$_m$-O-alkynyl, -(CH$_2$)$_m$-O-

$(CH_2)_m$-R_7, -$(CH_2)_m$-SH, -$(CH_2)_m$-S-alkyl, -$(CH_2)_m$-S-alkenyl, -$(CH_2)_m$-S-alkynyl, or -$(CH_2)_m$-S-$(CH_2)_m$-R_7,





R_7 represents, for each occurrence, a substituted or unsubstituted aryl, aralkyl, cycloalkyl, cycloalkenyl, or heterocycle;

R'_7 represents, for each occurrence, hydrogen, or a substituted or unsubstituted alkyl, alkenyl, aryl, aralkyl, cycloalkyl, cycloalkenyl or heterocyclyl;

R_8 and R_9 each independently represent hydrogen, alkyl, alkenyl, -$(CH_2)_m$-R_7, -C(=O)-alkyl, -C(=O)-alkenyl, -C(=O)-alkynyl, or -C(=O)-$(CH_2)_m$-R_7,

or R_8 and R_9 taken together with the N atom to which they are attached complete a heterocyclic ring having from 4 to 8 atoms in the ring structure;

R_{50} represents O or S;

R_{51} represents N_3, SH, NH_2, NO_2 or OR'_7;

R_{52} represents hydrogen, a lower alkyl, an amine, OR'_7, or a pharmaceutically acceptable salt, or R_{51} and R_{52} taken together with the phosphorous atom to which they are attached complete a heterocyclic ring having from 5 to 8 atoms in the ring structure;

Y_1 and Y_2 can independently or together be a group capable of being hydrolyzed to a hydroxyl group, or cyclic derivatives where Y_1 and Y_2 are connected via a ring having from 5 to 8 atoms in the ring structure;

X_1 represents a halogen;

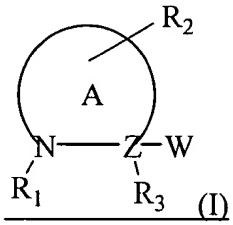
X_2 and X_3 each represent a hydrogen or a halogen;

m is zero or an integer in the range of 1 to 8; and n is an integer in the range of 1 to 8.

3. (Currently Amended) ~~A~~ The method of claim 2, wherein said ~~for modifying glucose metabolism of an animal, comprising administering to the animal a composition including~~ one or more protease inhibitors ~~which inhibit the proteolysis of glucagon-like peptide 1 (GLP-1) and~~

~~accordingly~~ increase the plasma half-life of GLP-1 in the animal. ~~wherein the inhibitor is represented by Formula I~~

4. (Currently Amended) A method for treating Type II diabetes, comprising administering to an animal a composition including one or more inhibitors of dipeptidylpeptidase IV (DPIV) represented by Formula I:



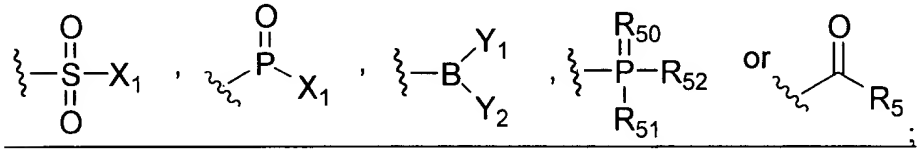
(I)

wherein

A represents a 4-8 membered heterocycle including the N and a Cα carbon;

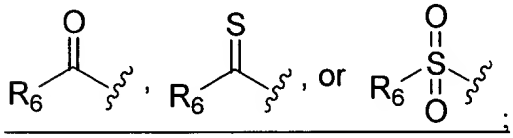
Z represents C or N;

W represents -CH=NR5,



;

R_1 represents a C-terminally linked amino acid residue or amino acid analog, or a C- terminally linked peptide or peptide analog, or an amino-protecting group, or



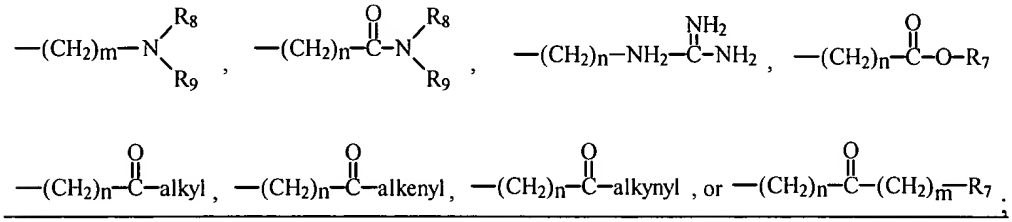
;

R_2 is absent or represents one or more substitutions to the ring A, each of which can independently be a halogen, a lower alkyl, a lower alkenyl, a lower alkynyl, a carbonyl, a thiocarbonyl, an amino, an acylamino, an amido, a cyano, a nitro, an azido, a sulfate, a sulfonate, a sulfonamido, $-(CH_2)_m-R_7$, $-(CH_2)_m-OH$, $-(CH_2)_m-O$-lower alkyl, $-(CH_2)_m-O$-lower alkenyl, $-(CH_2)_n-O-(CH_2)_m-R_7$, $-(CH_2)_m-SH$, $-(CH_2)_m-S$-lower alkyl, $-(CH_2)_m-S$-lower alkenyl, or $-(CH_2)_n-S-(CH_2)_m-R_7$;

if Z is N, R_3 represents hydrogen, if Z is C, R_3 represents hydrogen or a halogen, a lower alkyl, a lower alkenyl, a lower alkynyl, a carbonyl, a thiocarbonyl, an amino, an acylamino, an amido, a cyano, a nitro, an azido, a sulfate, a sulfonate, a sulfonamido, $-(CH_2)_m-R_7$, $-(CH_2)_m-OH$, $-(CH_2)_m-O$-lower alkyl, $-(CH_2)_m-O$-lower alkenyl, $-(CH_2)_n-O-(CH_2)_m-R_7$, $-(CH_2)_m-SH$, $-(CH_2)_m-S$-lower alkyl, $-(CH_2)_m-S$-lower alkenyl, or $-(CH_2)_n-S-(CH_2)_m-R_7$;

R_5 represents a hydrogen, an alkyl, an alkenyl, an alkynyl, $-C(X_1)(X_2)X_3$, $-(CH_2)_m-R_7$, $-(CH_2)_n-OH$, $-(CH_2)_n-O$-alkyl, $-(CH_2)_n-O$-alkenyl, $-(CH_2)_n-O$-alkynyl, $-(CH_2)_n-O-(CH_2)_m-R_7$, $-(CH_2)_n-SH$, $-(CH_2)_n-S$-alkyl, $-(CH_2)_n-S$-alkenyl, $-(CH_2)_n-S$-alkynyl, $-(CH_2)_n-S-(CH_2)_m-R_7$, $-C(O)C(O)NH_2$, or $-C(O)C(O)OR'_7$;

R_6 represents hydrogen, a halogen, an alkyl, an alkenyl, an alkynyl, an aryl, $-(CH_2)_m-R_7$, $-(CH_2)_m-OH$, $-(CH_2)_m-O$-alkyl, $-(CH_2)_m-O$-alkenyl, $-(CH_2)_m-O$-alkynyl, $-(CH_2)_m-O-(CH_2)_m-R_7$, $-(CH_2)_m-SH$, $-(CH_2)_m-S$-alkyl, $-(CH_2)_m-S$-alkenyl, $-(CH_2)_m-S$-alkynyl, or $-(CH_2)_m-S-(CH_2)_m-R_7$,



R_7 represents, for each occurrence, a substituted or unsubstituted aryl, aralkyl, cycloalkyl, cycloalkenyl, or heterocycle;

R'_7 represents, for each occurrence, hydrogen, or a substituted or unsubstituted alkyl, alkenyl, aryl, aralkyl, cycloalkyl, cycloalkenyl or heterocyclyl;

R_8 and R_9 each independently represent hydrogen, alkyl, alkenyl, $-(CH_2)_m-R_7$, $-C(=O)$-alkyl, $-C(=O)$-alkenyl, $-C(=O)$-alkynyl, or $-C(=O)-(CH_2)_m-R_7$,

or R_8 and R_9 taken together with the N atom to which they are attached complete a heterocyclic ring having from 4 to 8 atoms in the ring structure;

R_{50} represents O or S;

R_{51} represents N_3, SH, NH_2, NO_2 or OR'$_7$;

R_{52} represents hydrogen, a lower alkyl, an amine, OR'$_7$, or a pharmaceutically acceptable salt, or R_{51} and R_{52} taken together with the phosphorous atom to which they are attached complete a heterocyclic ring having from 5 to 8 atoms in the ring structure;

Y_1 and Y_2 can independently or together be a group capable of being hydrolyzed to a hydroxyl group, or cyclic derivatives where Y_1 and Y_2 are connected via a ring having from 5 to 8 atoms in the ring structure;

X_1 represents a halogen;

X_2 and X_3 each represent a hydrogen or a halogen;

m is zero or an integer in the range of 1 to 8; and n is an integer in the range of 1 to 8.

5. (Currently Amended) The method of claim 1 or 2, wherein the ~~dipeptidylpeptidase is DPIV~~animal is a mammal.

6. (Currently Amended) The method of claim ~~3~~5, wherein the ~~protease inhibitor is an inhibitor of DPIV~~mammal is a human.

7. (Previously Amended) The method of claim 2 or 3, wherein administering the inhibitor reduces one or more of insulin resistance, glucose intolerance, hyperglycemia, hyperinsulinemia, obesity, hyperlipidemia, or hyperlipoproteinemia.

8. (Previously Amended) The method of claim 1, 2, 3 or 4, wherein the inhibitor has an EC_{50} for modification of glucose metabolism which is at least one order of magnitude less than its EC_{50} for immunosuppression.

9. (Currently Amended) The method of claim 1, 2, 3 or 4, wherein the inhibitor has an EC_{50} for inhibition of glucose intolerance in the nanomolar or less range.

10. (Currently Amended) The method of claim 8, wherein the inhibitor has an EC_{50} for immunosuppression in the ~~μM~~micromolar or greater range.

11. (Previously Amended) The method of claim 4, ~~5~~ or 6, wherein the inhibitor has a Ki for DPIV inhibition of 1.0 nM or less.

12. (Previously Amended) The method of claim 1, 2, 3 or 4, wherein the inhibitor is peptidomimetic of a peptide selected from Pro-Pro, Ala-Pro, and (D)-Ala-(L)-Ala.

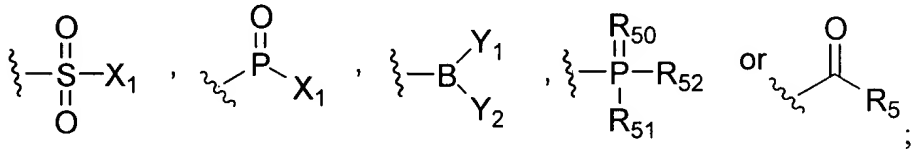
13. (Previously Amended) The method of claim 1, 2, 3 or 4, wherein the inhibitor has a molecular weight less than 7500 amu.

14. (Previously Amended) The method of claim 1, 2, 3 or 4, wherein the inhibitor is administered orally.

15. (Cancelled)

16. (Currently Amended) The method of claim 1, 2, 3, or 4, wherein

W represents $-CH=NR_5$,



;

R_5 represents H, an alkyl, an alkenyl, an alkynyl, $-C(X_1)(X_2)X_3$, $-(CH_2)m-R_7$, $-(CH_2)n-OH$, $-(CH_2)n-O-alkyl$, $-(CH_2)n-O-alkenyl$, $-(CH_2)n-O-alkynyl$, $-(CH_2)n-O-(CH_2)m-R_7$, $-(CH_2)n-SH$, $-(CH_2)n-S-alkyl$, $-(CH_2)n-S-alkenyl$, $-(CH_2)n-S-alkynyl$, $-(CH_2)n-S-(CH_2)m-R_7$, $-C(O)C(O)NH_2$, or $-C(O)C(O)OR'_7$;

R_7 represents, for each occurrence, a substituted or unsubstituted aryl, aralkyl, cycloalkyl, cycloalkenyl or heterocyclyl;

R'_7 represents, for each occurrence, hydrogen, or a substituted or unsubstituted alkyl, alkenyl, aryl, aralkyl, cycloalkyl, cycloalkenyl, or heterocycle;

Y_1 and Y_2 can independently or together be OH, or a group capable of being hydrolyzed to a hydroxyl group, ~~including~~ or cyclic derivatives where Y_1 and Y_2 are connected via a ring having from 5 to 8 atoms in the ring structure;

R_{50} represents O or S;

R_{51} represents N_3, SH, NH_2, NO_2 or OR'7;

R_{52} represents hydrogen, a lower alkyl, an amine, OR'7, or a pharmaceutically acceptable salt, or R_{51} and R_{52} taken together with the phosphorous atom to which they are attached complete a heterocyclic ring having from 5 to 8 atoms in the ring structure;

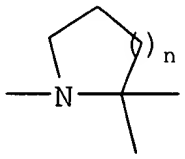
X_1 represents a halogen;

X_2 and X_3 each represent a hydrogen or a halogen;

m is zero or an integer in the range of 1 to 8; and

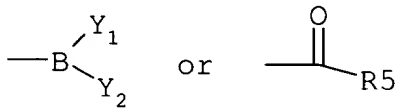
n is an integer in the range of 1 to 8.

17. (Previously Amended) The method of claim 16, wherein the ring A is represented by the formula:

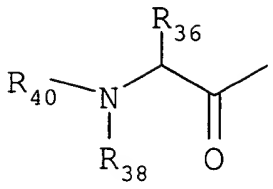


wherein n is an integer of 1 or 2.

18. (Previously Amended) The method of claim 16, wherein W represents



19. (Original) The method of claim 16, wherein R_1 represents



R_{36} is a small hydrophobic group and R_{38} is hydrogen, or, R_{36} and R_{38} together form a 4-7 membered heterocycle including the N and the Cα carbon, as defined for A above; and

R_{40} represents a C-terminally linked amino acid residue or amino acid analog, or a C-terminally linked peptide or peptide analog, or an amino-protecting group.

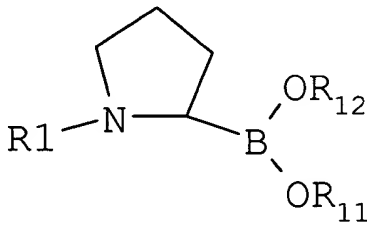
20. (Previously Amended) The method of claim 16, wherein R_2 is absent, or represents a small hydrophobic group.

21. (Previously Amended) The method of claim 16, wherein R_3 is a hydrogen, or a small hydrophobic group.

22. (Previously Amended) The method of claim 16, wherein R_5 is a hydrogen, or a halogenated lower alkyl.

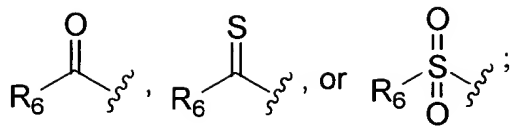
23. (Previously Amended) The method of claim 16, wherein X_1 is a fluorine, and X_2 and X_3, if halogens, are fluorine.

24. (Currently Amended) The method of claim 16, wherein the inhibitor is represented by the general formula:

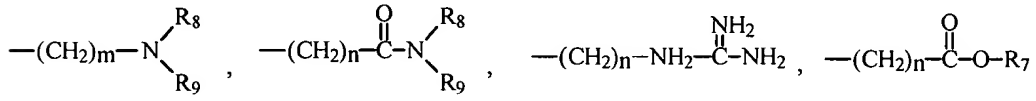


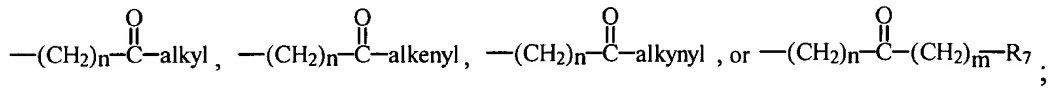
wherein

R_1 represents a C-terminally linked amino acid residue or amino acid analog, or a C-terminally linked peptide or peptide analog, or an amino protecting group, or



R_6 represents hydrogen, a halogen, an alkyl, an alkenyl, an alkynyl, an aryl, -$(CH_2)_m$-R_7, -$(CH_2)_m$-OH, -$(CH_2)_m$-O-alkyl, -$(CH_2)_m$-O-alkenyl, -$(CH_2)_m$-O-alkynyl, -$(CH_2)_m$-O-$(CH_2)_m$-R_7, -$(CH_2)_m$-SH, -$(CH_2)_m$-S-alkyl, -$(CH_2)_m$-S-alkenyl, -$(CH_2)_m$-S-alkynyl, -$(CH_2)_m$-S-$(CH_2)_m$-R_7,





R_7 represents an aryl, a cycloalkyl, a cycloalkenyl, or a heterocycle;

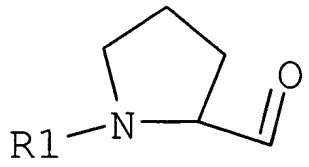
R_8 and R_9 each independently represent hydrogen, alkyl, alkenyl, -$(CH_2)_m$-R_7, -C(=O)-alkyl, -C(=O)-alkenyl, -C(=O)-alkynyl, or -C(=O)-$(CH_2)_m$-R_7,

or R_8 and R_9 taken together with the N atom to which they are attached complete a heterocyclic ring having from 4 to 8 atoms in the ring structure;

R_{11} and R_{12} each independently represent hydrogen, an alkyl, or a pharmaceutically acceptable salt, or R_{11} and R_{12} taken together with the O-B-O atoms to which they are attached complete a heterocyclic ring having from 5 to 8 atoms in the ring structure;

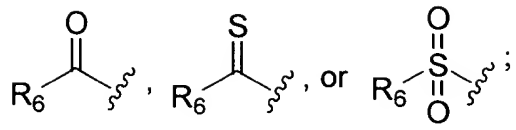
m is zero or an integer in the range of 1 to 8; and n is an integer in the range of 1 to 8.

25. (Currently Amended) The method of claim 16, wherein the inhibitor is represented by the general formula

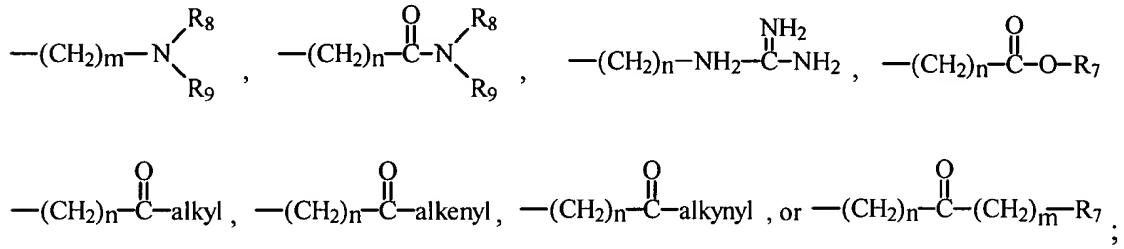


wherein

R_1 represents a C-terminally linked amino acid residue or amino acid analog, or a C-terminally linked peptide or peptide analog, or an amino protecting group, or



R_6 represents hydrogen, a halogen, an alkyl, an alkenyl, an alkynyl, an aryl, -$(CH_2)_m$-R_7, -$(CH_2)_m$-OH, -$(CH_2)_m$-O-alkyl, -$(CH_2)_m$-O-alkenyl, -$(CH_2)_m$-O-alkynyl, -$(CH_2)_m$-O-$(CH_2)_m$-R_7, -$(CH_2)_m$-SH, -$(CH_2)_m$-S-alkyl, -$(CH_2)_m$-S-alkenyl, -$(CH_2)_m$-S-alkynyl, -$(CH_2)_m$-S-$(CH_2)_m$-R_7,



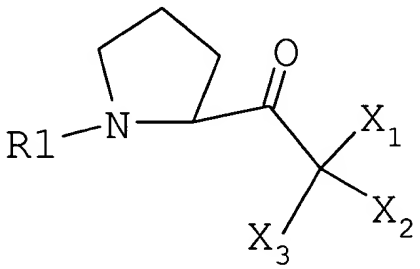
R_7 represents an aryl, a cycloalkyl, a cycloalkenyl, or a heterocycle;

R_8 and R_9 each independently represent hydrogen, alkyl, alkenyl, -$(CH_2)_m$-R_7, -C(=O)-alkyl, -C(=O)-alkenyl, -C(=O)-alkynyl, or -C(=O)-$(CH_2)_m$-R_7,

or R_8 and R_9 taken together with the N atom to which they are attached complete a heterocyclic ring having from 4 to 8 atoms in the ring structure;

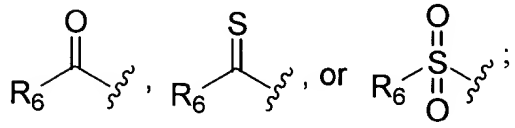
m is zero or an integer in the range of 1 to 8; and n is an integer in the range of 1 to 8.

26. (Currently Amended) The method of claim 16, wherein the inhibitor is represented by the general formula:

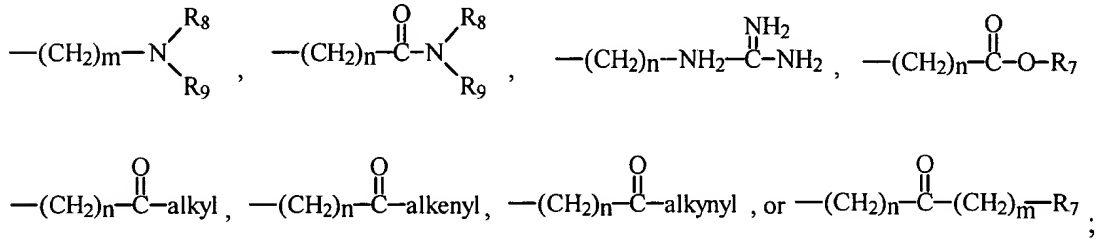


wherein

R_1 represents a C-terminally linked amino acid residue or amino acid analog, or a C-terminally linked peptide or peptide analog, or an amino protecting group, or



R_6 represents hydrogen, a halogen, an alkyl, an alkenyl, an alkynyl, an aryl, $-(CH_2)_m-R_7$, $-(CH_2)_m-OH$, $-(CH_2)_m-O-alkyl$, $-(CH_2)_m-O-alkenyl$, $-(CH_2)_m-O-alkynyl$, $-(CH_2)_m-O-(CH_2)_m-R_7$, $-(CH_2)_m-SH$, $-(CH_2)_m-S-alkyl$, $-(CH_2)_m-S-alkenyl$, $-(CH_2)_m-S-alkynyl$, $-(CH_2)_m-S-(CH_2)_m-R_7$,



R_7 represents an aryl, a cycloalkyl, a cycloalkenyl, or a heterocycle;

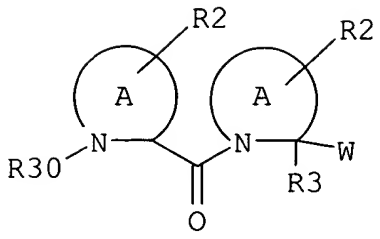
R_8 and R_9 each independently represent hydrogen, alkyl, alkenyl, $-(CH_2)_m-R_7$, -C(=O)-alkyl, -C(=O)-alkenyl, -C(=O)-alkynyl, or -C(=O)-$(CH_2)_m-R_7$,

or R_8 and R_9 taken together with the N atom to which they are attached complete a heterocyclic ring having from 4 to 8 atoms in the ring structure;

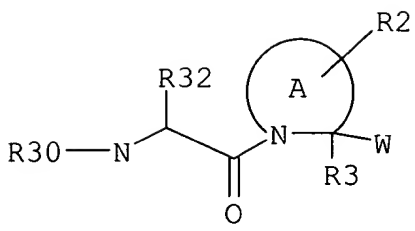
X_1, X_2 and X_3 each represent ~~a hydrogen or~~ a halogen;

m is zero or an integer in the range of 1 to 8; and n is an integer in the range of 1 to 8.

27. (Currently Amended) The method of claim 16, wherein the inhibitor is represented by the general formula:

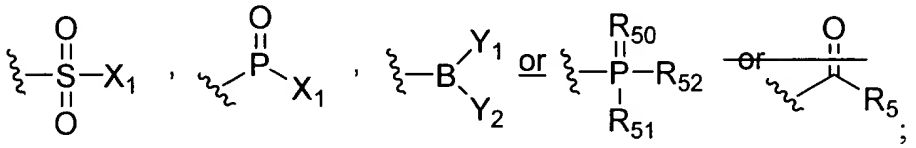


or



wherein
A represent a 4-8 membered heterocycle including an N and a Cα carbon;

W represents, ~~-CH=NR5;~~



R_2 is absent or represents one or more substitutions to the ring A, each of which can independently be a halogen, a lower alkyl, a lower alkenyl, a lower alkynyl, a carbonyl, a thiocarbonyl, an amino, an acylamino, an amido, a cyano, a nitro, an azido, a sulfate, a sulfonate, a sulfonamido, $-(CH_2)_m-R_7$, $-(CH_2)_m-OH$, $-(CH_2)_m-O$-lower alkyl, $-(CH_2)_m-O$-lower alkenyl, $-(CH_2)_n-O-(CH_2)_m-R_7$, $-(CH_2)_m-SH$, $-(CH_2)_m-S$-lower alkyl, $-(CH_2)_m-S$-lower alkenyl, or $-(CH_2)_n-S-(CH_2)_m-R_7$;

R_3 represents a hydrogen or a halogen, a lower alkyl, a lower alkenyl, a lower alkynyl, a carbonyl, a thiocarbonyl, an amino, an acylamino, an amido, a cyano, a nitro, an azido, a sulfate, a sulfonate, a sulfonamido, $-(CH_2)_m-R_7$, $-(CH_2)_m-OH$, $-(CH_2)_m-O$-lower alkyl, $-(CH_2)_m-O$-lower alkenyl, $-(CH_2)_n-O-(CH_2)_m-R_7$, $-(CH_2)_m-SH$, $-(CH_2)_m-S$-lower alkyl, $-(CH_2)_m-S$-lower alkenyl, or $-(CH_2)_n-S-(CH_2)_m-R_7$;

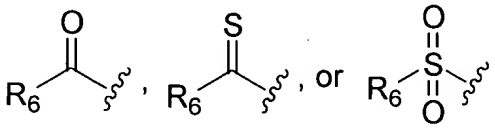
R_5 represents a hydrogen, an alkyl, an alkenyl, an alkynyl, $-C(X_1)(X_2)X_3$, $-(CH_2)_m-R_7$, $-(CH_2)_n-OH$, $-(CH_2)_n-O$-alkyl, $-(CH_2)_n-O$-alkenyl, $-(CH_2)_n-O$-alkynyl, $-(CH_2)_n-O-(CH_2)_m-R_7$, $-(CH_2)_n-SH$, $-(CH_2)_n-S$-alkyl, $-(CH_2)_n-S$-alkenyl, $-(CH_2)_n-S$-alkynyl, $-(CH_2)_n-S-(CH_2)_m-R_7$, $-C(O)C(O)NH_2$, or $-C(O)C(O)OR'_7$;

R_7 represents, for each occurrence, a substituted or unsubstituted aryl, aralkyl, cycloalkyl, cycloalkenyl or heterocyclyl;

R'_7 represents, for each occurrence, hydrogen, or a substituted or unsubstituted alkyl, alkenyl, aryl, aralkyl, cycloalkyl, cycloalkenyl or heterocyclyl;

R_{32} is a small hydrophobic group;

R_{30} represents a C-terminally linked amino acid residue or amino acid analog, or a C-terminally linked peptide or peptide analog, or an amino-protecting group; or



R_{50} represents O or S;

R_{51} represents N_3, SH, NH_2, NO_2 or OR'_7;

R_{52} represents hydrogen, a lower alkyl, an amine, OR'_7, or a pharmaceutically acceptable salt, or R_{51} and R_{52} taken together with the phosphorous atom to which they are attached complete a heterocyclic ring having from 5 to 8 atoms in the ring structure;

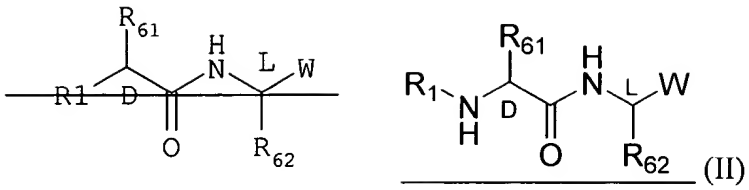
X_1 represents a halogen;

X_2 and X_3 each represent a hydrogen or a halogen;

m is zero or an integer in the range of 1 to 8; and

n is an integer in the range of 1 to 8.

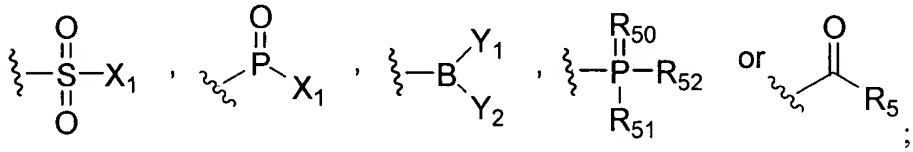
28. (Currently Amended) A method for modifying, in an animal, metabolism of glucagon-like peptide 1 (GLP-1), comprising administering to the animal a composition including one or more inhibitors of a dipeptidylpeptidase which inactivates GLP-1,, wherein the inhibitor is represented by Formula II:



(II)

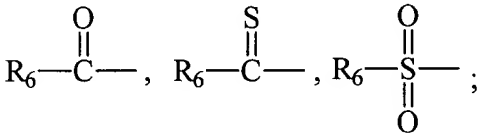
wherein

W represents a functional group which reacts with an active site residue of the targeted protease, selected from -CN, -CH=NR$_5$,



;

R_1 represents a C-terminally linked amino acid residue or amino acid analog, or a C- terminally linked peptide or peptide analog, or an amino-protecting group, or



;

R_3 represents hydrogen or a halogen, a lower alkyl, a lower alkenyl, a lower alkynyl, a carbonyl, a thiocarbonyl, an amino, an acylamino, an amido, a cyano, a nitro, an azido, a sulfate, a sulfonate, a sulfonamido, -$(CH_2)_m$-R_7, -$(CH_2)_m$-OH, -$(CH_2)_m$-O-lower alkyl, -$(CH_2)_m$-O-lower alkenyl, -$(CH_2)_n$-O-$(CH_2)_m$-R_7, -$(CH_2)_m$-SH, -$(CH_2)_m$-S-lower alkyl, -$(CH_2)_m$-S-lower alkenyl, or -$(CH_2)_n$-S-$(CH_2)_m$-R_7;

R_5 represents H, an alkyl, an alkenyl, an alkynyl, -$C(X_1)(X_2)X_3$, -(CH_2)m-R_7, -(CH_2)n-OH, -(CH_2)n-O-alkyl, -(CH_2)n-O-alkenyl, -(CH_2)n-O-alkynyl, -(CH_2)n-O-(CH_2)m-R_7, -(CH_2)n-SH, -(CH_2)n-S-alkyl, -(CH_2)n-S-alkenyl, -(CH_2)n-S-alkynyl, -(CH_2)n-S-(CH_2)m-R_7, -C(O)C(O)NH_2, or -C(O)C(O)OR'$_7$;

R_6 represents hydrogen, a halogen, an alkyl, an alkenyl, an alkynyl, an aryl, -$(CH_2)_m$-R_7, -$(CH_2)_m$-OH, -$(CH_2)_m$-O-alkyl, -$(CH_2)_m$-O-alkenyl, -$(CH_2)_m$-O-alkynyl, -$(CH_2)_m$-O-

$(CH_2)_m$-R_7, -$(CH_2)_m$-SH, -$(CH_2)_m$-S-alkyl, -$(CH_2)_m$-S-alkenyl, -$(CH_2)_m$-S-alkynyl, or -$(CH_2)_m$-S-$(CH_2)_m$-R_7;

R_7 represents, for each occurrence, a substituted or unsubstituted aryl, aralkyl, cycloalkyl, cycloalkenyl, or heterocycle;

R'_7 represents, for each occurrence, hydrogen, or a substituted or unsubstituted alkyl, alkenyl, aryl, aralkyl, cycloalkyl, cycloalkenyl, or heterocycle;

R_{61} and R_{62}, independently, represent small hydrophobic groups;

Y_1 and Y_2 can independently or together be OH, or a group capable of being hydrolyzed to a hydroxyl group, ~~including~~or cyclic derivatives where Y_1 and Y_2 are connected via a ring having from 5 to 8 atoms in the ring structure ;

R_{50} represents O or S;

R_{51} represents N_3, SH, NH_2, NO_2 or OR'_7;

R_{52} represents hydrogen, a lower alkyl, an amine, OR'_7, or a pharmaceutically acceptable salt, or R_{51} and R_{52} taken together with the phosphorous atom to which they are attached complete a heterocyclic ring having from 5 to 8 atoms in the ring structure;

X_1 represents a halogen;

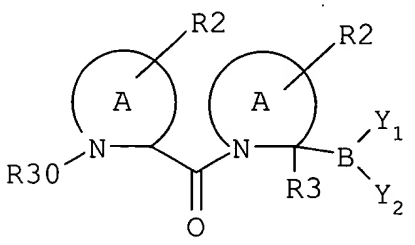
X_2 and X_3 each represent a hydrogen or a halogen;

m is zero or an integer in the range of 1 to 8; and n is an integer in the range of 1 to 8.

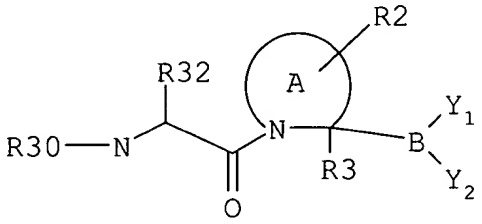
29. (Currently Amended) A method for ~~modifiying~~modifying, in an animal, metabolism of peptide hormone, comprising administering to the animal a composition including one or more boronyl peptidomimetic inhibitors of dipeptidylpeptidase IV (DPIV) in an amount sufficient to increase the plasma half-life of a peptide hormone, which peptide hormone is selected from ~~the group consisting of~~ glucagon-like peptide 2 (GLP-2), growth hormone-releasing factor (GHRF), vasoactive intestinal peptide (VIP), peptide histidine isoleucine (PHI), pituitary adenylate cyclase activating peptide (PACAP), gastric inhibitory peptide (GIP), helodermin, Peptide YY and neuropeptide Y.

30. (Currently Amended) A method for modifying glucose metabolism of an animal, comprising administering to the animal a composition including a boronyl peptidomimetic of a peptide selected from Pro-Pro, Ala-Pro, and (D)-Ala-(L)-Ala.

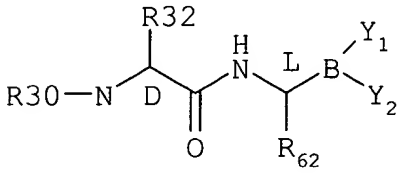
31. (Currently Amended) The method of claim ~~31~~30, wherein the boronyl peptidomimetic is represented in the general formula:



or



or



wherein

each A independently represents a 4-8 membered heterocycle including the N and a Cα carbon;

R_2 is absent or represents one or more substitutions to the ring A, each of which can independently be a halogen, a lower alkyl, a lower alkenyl, a lower alkynyl, a carbonyl, a thiocarbonyl, an amino, an acylamino, an amido, a cyano, a nitro, an azido, a sulfate, a sulfonate, a sulfonamido, $-(CH_2)_m-R_7$, $-(CH_2)_m-OH$, $-(CH_2)_m-O$-lower alkyl, $-(CH_2)_m-O$-lower alkenyl, $-(CH_2)_n-O-(CH_2)_m-R_7$, $-(CH_2)_m-SH$, $-(CH_2)_m-S$-lower alkyl, $-(CH_2)_m-S$-lower alkenyl, or $-(CH_2)_n-S-(CH_2)_m-R_7$;

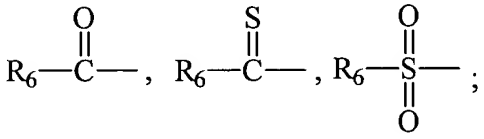
R_3 represents hydrogen or a halogen, a lower alkyl, a lower alkenyl, a lower alkynyl, a carbonyl, a thiocarbonyl, an amino, an acylamino, an amido, a cyano, a nitro, an azido, a sulfate, a sulfonate, a sulfonamido, $-(CH_2)_m-R_7$, $-(CH_2)_m-OH$, $-(CH_2)_m-O$-lower alkyl, $-(CH_2)_m-O$-lower alkenyl, $-(CH_2)_n-O-(CH_2)_m-R_7$, $-(CH_2)_m-SH$, $-(CH_2)_m-S$-lower alkyl, $-(CH_2)_m-S$-lower alkenyl, or $-(CH_2)_n-S-(CH_2)_m-R_7$;

~~R_5 represents H, an alkyl, an alkenyl, an alkynyl, $-C(X_1)(X_2)X_3$, $-(CH_2)_m-R_7$, $-(CH_2)_n-OH$, $-(CH_2)_n-O$-alkyl, $-(CH_2)_n-O$-alkenyl, $-(CH_2)_n-O$-alkynyl, $-(CH_2)_n-O-(CH_2)_m-R_7$, $-(CH_2)_n-SH$, $-(CH_2)_n-S$-alkyl, $-(CH_2)_n-S$-alkenyl, $-(CH_2)_n-S$-alkynyl, $-(CH_2)_n-S-(CH_2)_m-R_7$, $-C(O)C(O)NH_2$, or $-C(O)C(O)OR'_7$;~~

R_6 represents hydrogen, a halogen, an alkyl, an alkenyl, an alkynyl, an aryl, $-(CH_2)_m-R_7$, $-(CH_2)_m-OH$, $-(CH_2)_m-O$-alkyl, $-(CH_2)_m-O$-alkenyl, $-(CH_2)_m-O$-alkynyl, $-(CH_2)_m-O-(CH_2)_m-R_7$, $-(CH_2)_m-SH$, $-(CH_2)_m-S$-alkyl, $-(CH_2)_m-S$-alkenyl, $-(CH_2)_m-S$-alkynyl, or $-(CH_2)_m-S-(CH_2)_m-R_7$;

R_7 represents, for each occurrence, a substituted or unsubstituted aryl, aralkyl, cycloalkyl, cycloalkenyl, or heterocycle;

R_{30} represents a C-terminally linked amino acid residue or amino acid analog, or a C- terminally linked peptide or peptide analog, or an amino-protecting group, or



R_{32} and ~~R_{61}~~R_{62}, independently, represent small hydrophobic groups;

Y_1 and Y_2 can independently or together be OH, or a group capable of being hydrolyzed to a hydroxyl group, ~~including~~or cyclic derivatives where Y_1 and Y_2 are connected via a ring having from 5 to 8 atoms in the ring structure ;

m is zero or an integer in the range of 1 to 8; and n is an integer in the range of 1 to 8.

32. (Currently Amended) The method of claim 31, wherein administering the boronyl peptidomimetic reduces one or more of insulin resistance, glucose intolerance, hyperglycemia, hyperinsulinemia, obesity, hyperlipidemia, or hyperlipoproteinemia.

33. (Previously Amended) The method of claim 31, wherein the boronyl peptidomimetic has an EC_{50} for modification of glucose metabolism which is at least one order of magnitude less than its EC_{50} for immunosuppression.

34. (Previously Amended) The method of claim 31, wherein the boronyl peptidomimetic has an EC_{50} for inhibition of glucose tolerance in the nanomolar or less range.

35. (Previously Amended) The method of claim 31, wherein the boronyl peptidomimetic has an EC_{50} for immunosuppression in the μM or greater range.

36. (Previously Amended) The method of claim 31, wherein the boronyl peptidomimetic is administered orally.

37. (Currently Amended) A method for modifying glucose metabolism of an animal, comprising administering to the animal a composition comprising a peptidomimetic boronyl inhibitor wherein the peptide to be mimicked is Pro-Pro, Ala-Pro, ~~and~~ or (D)-Ala-(L)-Ala.

38. (New) The method of claim 6, wherein the human is a Type II diabetic.